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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,181	01/10/2002	Geoffrey Phillip Dobson	FREE001	6148

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EXAMINER
DAVIS, RUTH A

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,181	DOBSON, GEOFFREY PHILLIP	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-8 and 44-93 is/are pending in the application.

4a) Of the above claim(s) 1-8 and 44-76 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 77-93 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-8,44-93 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3,8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1 – 8 and 44 – 76, drawn to a method for preserving organs.

Group II, claims 77 – 93, drawn to a pharmaceutical composition.

2. The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: There is no special technical feature that contributes over the art. For example, compositions of adenosine and lidocaine are known in the art, as demonstrated in the cited references below.

3. During a telephone conversation with Carol LaSalle on January 31, 2003, a provisional election was made without traverse to prosecute the invention of II, claim77 - 93. Affirmation of this election must be made by applicant in replying to this Office action.

Claims 1 – 8 and 44 – 76 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

4. Claims 80 and 81 are objected to because of the following informalities: The term "mipivacaine" should be spelled correctly as "mepivacaine". Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 81 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 81 is drawn to a pharmaceutical composition however is rendered indefinite because it is unclear if the claim is intended to depend from claim 77, as it is a duplicate of claim 80.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 77 – 78, 80 – 83 and 90 are rejected under 35 U.S.C. 102(b) as being anticipated by Antropoli (WO 98/37886).

Applicant claims a pharmaceutical or veterinarian composition comprising effective amounts of (i) potassium channel opener, an agonist thereof, or an adenosine receptor agonist; and (ii) a local anaesthetic. The potassium channel opener or agonist thereof is selected from a named group; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mipivacaine and class 1B antiarrhythmic agents. The composition is administered together with an acceptable carrier, diluent, adjuvant or excipient, or alternatively with another medicament. The composition is a cardioplegic or cardioprotectant composition.

Antropoli teaches compositions comprising nifedipine (potassium channel opener), and lidocaine (local anesthetic, class 1B antiarrhythmic agent) or carbocaine (local anesthetic) (abstract). The composition may further contain other drugs (abstract), carriers and excipients (claims).

Although Antropoli does not specifically teach the composition is a cardioplegic, the compositions are the same. Therefore, the composition of Antropoli must inherently act as a cardioplegic.

The reference anticipates the claimed subject matter.

9. Claims 77 – 78, 80 – 83 and 93 are rejected under 35 U.S.C. 102(b) as being anticipated by Homeister et al. (1990).

Applicant claims a pharmaceutical or veterinarian composition comprising effective amounts of (i) potassium channel opener, an agonist thereof, or an adenosine receptor agonist;

and (ii) a local anaesthetic. The potassium channel opener or agonist thereof is selected from a named group, specifically AV blocker adenosine; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mipivacaine and class 1B antiarrhythmic agents. The composition is administered together with an acceptable carrier, diluent, adjuvant or excipient. Finally the composition is a cardioplegic or cardioprotectant composition.

Homeister teaches compositions comprising adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic) for controlling myocardial injury (abstract) administered with saline (p.597).

Although Homeister does not specifically teach the composition is cardioplegic, the compositions are the same. Therefore, the composition of Homeister must inherently act as a cardioplegic.

The reference anticipates the claimed subject matter.

10. Claims 77 – 78, 80 – 83, 90 and 93 are rejected under 35 U.S.C. 102(b) as being anticipated by Garratt et al. (AHJ)

Applicant claims a pharmaceutical or veterinarian composition comprising effective amounts of (i) potassium channel opener, an agonist thereof, or an adenosine receptor agonist; and (ii) a local anaesthetic. The potassium channel opener or agonist thereof is selected from a named group, specifically AV blocker adenosine; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mipivacaine and class 1B antiarrhythmic agents. The composition is administered together with an acceptable carrier, diluent, adjuvant or

excipient; or alternatively with another medicament. Finally the composition is a cardioplegic or cardioprotectant composition.

Garratt teaches a composition of adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic) and it's benefit in patients with myocardial infarctions (abstract). Garratt teaches the addition of adenosine and lidocaine to cardioplegic solutions reduces ventricular dysfunction and has similar benefits for myocardial infarction (p.196). Other medicaments for managing myocardial infarction were (aspirin, beta-blockers) were co-administered (p.197).

The reference anticipates the claimed subject matter.

11. Claims 77 – 78, 80 – 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Jayawant et al. (1998).

Applicant claims a pharmaceutical or veterinarian composition comprising effective amounts of (i) potassium channel opener, an agonist thereof, or an adenosine receptor agonist; and (ii) a local anaesthetic. The potassium channel opener or agonist thereof is selected from a named group; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mipivacaine and class 1B antiarrhythmic agents. The composition is administered together with an acceptable carrier, diluent, adjuvant or excipient; specifically a buffer with a pH of about 6 – 9; more specifically wherein the buffer is Krebs-Henseleit, St. Thomas No.2 solution, Tyrodes solutions, Fremes solution, Hartmanns solution of Ringers-Lactate. Further, the carrier has low concentrations of potassium of up to about 10 mM and low concentrations of magnesium up to about 2.5 mM. Finally, the composition is a cardioplegic or cardioprotectant composition.

Jayawant teaches cardioplegic compositions of Krebs-Henseleit and pinacidil, wherein the infusions contain procaine (abstract, p.133). Jaywant teaches pinacidil is administered with Krebs-Henseleit as a delivery medium (p.133).

Although Jayawant does not specifically teach the buffer has a pH of 6 – 9, the buffers used are those as claimed, therefore they must have a pH of 6 – 9. Furthermore, although Jayawant does not teach the compositions wherein the carrier has up to 10mM potassium or up to 2.5mM magnesium, Krebs-Henseleit was known to have these amounts of potassium and magnesium. (See Raymond US 5693462, Table 1.)

The reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 77 – 78 and 80 – 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jayawant.

Applicant claims a pharmaceutical or veterinarian composition comprising effective amounts of (i) potassium channel opener, an agonist thereof, or an adenosine receptor agonist; and (ii) a local anaesthetic. The potassium channel opener or agonist thereof is selected from a

named group; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mipivacaine and class 1B antiarrhythmic agents. The composition is administered together with an acceptable carrier, diluent, adjuvant or excipient. Specifically, a buffer with a pH of about 6 – 9 selected from Krebs-Henseleit, St. Thomas No.2 solution, Tyrodes solutions, Fremes solution, Hartmanns solution of Ringers-Lactate. The carrier, diluent, adjuvant or excipient has low concentrations of potassium, up to about 10 mM; and low concentrations of magnesium, up to about 2.5 mM. Finally, the composition is a cardioplegic or cardioprotectant composition.

Jayawant teaches cardioplegic compositions of Krebs-Henseleit and pinacidil, wherein the infusions contain procaine (abstract, p.133). Jaywant teaches pinacidil is administered with Krebs-Henseleit as a delivery medium (p.133). Although Jayawant does not specifically teach the buffer has a pH of 6 – 9, the buffers used are those as claimed, therefore they must have a pH of 6 – 9. Furthermore, although Jayawant does not teach the compositions wherein the carrier has up to 10mM potassium or up to 2.5mM magnesium, Krebs-Henseleit was known to have these amounts of potassium and magnesium. In support, Raymond (US 5693462) teaches Krebs-Henseleit contains 3 – 30mM potassium and 0.9 – 4.8mM magnesium (Table 1).

Jayawant does not teach each of the claimed potassium channel openers or buffers in the compositions. However, Jayawant does teach that potassium channel openers, Krebs-Henseleit solution, and St. Thomas' Hospital solution are effective cardioplegic agents (p.132, abstract). Therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Jayawant to substitute other potassium channel openers and buffers in the disclosed

composition with a reasonable expectation for successfully obtaining an effective cardioplegic composition.

14. Claims 77 – 78, 80 – 83 and 90 – 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garratt in view of Glasser et al. (US 5256770).

Applicant claims a pharmaceutical or veterinarian composition comprising effective amounts of (i) potassium channel opener, an agonist thereof, or an adenosine receptor agonist; and (ii) a local anaesthetic. The potassium channel opener or agonist thereof is selected from a named group, specifically AV blocker adenosine; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mipivacaine and class 1B antiarrhythmic agents. The composition is administered together with an acceptable carrier, diluent, adjuvant or excipient; or alternatively with another medicament, specifically dipyridamole or streptokinase. Finally the composition is a cardioplegic or cardioprotectant composition.

Garratt teaches a composition of adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic) and it's benefit in patients with acute myocardial infarctions (abstract). Garratt teaches the addition of adenosine and lidocaine to cardioplegic solutions reduces ventricular dysfunction and has similar benefits for myocardial infarction (p.196). Other medicaments for managing myocardial infarction were (aspirin, beta-blockers) were co-administered (p.197).

Garratt does not teach the compositions wherein the additional medicaments co-administered were dipyridamol or streptokinase. However, Glasser teaches that streptokinase is commonly used to treat acute myocardial infarction (col.9 line 5-12). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Glasser to combine

streptokinase to the composition of Garratt because of its known use in managing acute myocardial infarction. Further, it would have been obvious to one of ordinary skill in the art to combine streptokinase, adenosine and lidocaine for their common benefit as cited by the references above. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine streptokinase, adenosine and lidocaine together with a reasonable expectation for successfully obtaining a composition effective for treating acute myocardial infarction.

15. Claims 77 – 83 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garratt or Homeister.

Applicant claims a pharmaceutical or veterinarian composition comprising effective amounts of (i) potassium channel opener, an agonist thereof, or an adenosine receptor agonist; and (ii) a local anaesthetic. The potassium channel opener or agonist thereof is selected from a named group; and the adenosine receptor agonist is selected from a named group. The local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mipivacaine and class 1B antiarrhythmic agents. The composition is administered together with an acceptable carrier, diluent, adjuvant or excipient. Finally, the composition is a cardioplegic or cardioprotectant composition.

Garratt teaches a composition of adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic) and it's benefit in patients with acute myocardial infarctions (abstract). Garratt teaches the addition of adenosine and lidocaine to cardioplegic solutions reduces ventricular

dysfunction and has similar benefits for myocardial infarction (p.196). Other medicaments for managing myocardial infarction (aspirin, beta-blockers) were co-administered (p.197).

Homeister teaches compositions comprising adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic) for controlling myocardial injury (abstract) administered with saline (p.597). Although Homeister does not specifically teach the composition is cardioplegic, the compositions are the same. Therefore, the composition of Homeister must inherently act as a cardioplegic.

The references do not teach the compositions wherein an adenosine receptor agonist is used. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use an analogue or agonist of adenosine in the reference compositions as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to use agonists/analogues of adenosine in the reference compositions with a reasonable expectation for successfully obtaining a composition effective for treating myocardial conditions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
March 11, 2003

LEON B. LANKFORD, JR.
PRIMARY EXAMINER